

Adducts of Anthrahydroquinone and Anthranol with Lignin Model Quinone Methides. 3. Independent Synthesis of Threo and Erythro Isomers[†]

John Ralph

Forest Research Institute, Private Bag, Rotorua, New Zealand

Lawrence L. Landucci*[‡]

Forest Products Laboratory, Forest Service, U.S. Department of Agriculture, Madison, Wisconsin 53705

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A key intermediate responsible for anthrahydroquinone- (AHQ-) catalyzed delignification of wood under alkaline conditions is an adduct between AHQ and a quinone methide (QM) of a phenylpropanoid lignin subunit represented by models such as 1-(3-methoxy-4-hydroxyphenyl)-2-(2-methoxyphenoxy)propane-1,3-diol. Unlike adduct formation via QMs, which give only threo products with AHQ or anthranol (9-hydroxyanthracene), both isomers were successfully prepared by alkylating 9,10-bis(trimethylsiloxy)anthracene or 9-(trimethylsiloxy)anthracene with α -bromo derivatives of lignin models in the presence of the Lewis acid zinc bromide. It is demonstrated by ¹H NMR spectroscopy that the solution conformations of erythro adducts are markedly different from those of the threo adducts and that the conformations vary with substitution and changes in solvent. Also, the erythro isomers are relatively unstable and readily isomerize under the alkylation conditions.

During a study¹ of intermediates involved in the catalytic delignification of wood, adducts **1a-d** (Figure 1) were synthesized by the reaction of anthranol or anthrahydroquinone (AHQ) with lignin model quinone methides followed by methylation (Scheme I). Interestingly, only the threo² diastereomer was found for each adduct prepared. This assignment has since been confirmed on the basis of NMR studies of dehydration derivatives.³

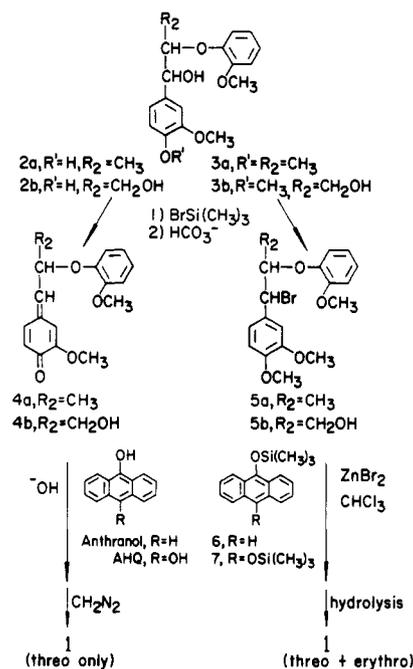
In this study, erythro as well as threo isomers were synthesized by allowing the trimethylsilyl (Me₃Si) ethers of anthranol or AHQ (**6** and **7**, Scheme I) to react with the benzyl bromides **5a** and **5b** in the presence of a Lewis acid catalyst (Scheme I). Synthesis of silyl enol ethers and subsequent alkylation with benzyl halides have been described.^{4,5} Presumably, the alkylation proceeds via an intermediate benzylic carbonium ion as evidenced by rapid isomerization of *threo*-**5a**⁶ or **-5b** to a 53:47 threo/erythro mixture in the presence of zinc bromide.⁷

Anthranol Adducts. Alkylation of (trimethylsilyl)-anthranol (**6**) with **5a** gave both isomers of the expected adduct **1a** in a combined yield of more than 95% before purification.⁸ Proton NMR monitoring of the reaction indicated that adduct formation was complete within 2 min after addition of the Lewis acid catalyst and that the erythro isomer was isomerizing to the threo isomer. From an initial threo/erythro ratio of approximately 3:2, complete isomerization to the threo isomer occurred within 4 h at room temperature. Similarly, alkylation of **6** with **5b** gave a quantitative yield of **1b** with a threo/erythro ratio of 2:1.

The respective isomers were compared by mass, infrared, ¹³C NMR, and ¹H NMR spectroscopies. The electron-impact mass spectra of the threo and erythro isomers of each compound contain the same M⁺ peak and fragmentation peaks with slightly different relative intensities; the infrared spectra are slightly different in the fingerprint region; and the ¹³C NMR spectra are consistent with their isomeric nature, as exemplified by minor differences in chemical shifts.

The most informative comparison was made by ¹H NMR spectroscopy, which indicates a notable difference in the location of the dimethoxyphenyl moiety (ring A)

Scheme I



relative to the anthracenyl moiety (Figure 2) between the threo and erythro forms. As previously described,^{1,3} the characteristic conformation of threo-AHQ and anthranol adducts was relatively insensitive to substituent effects and was based primarily on the intense shielding of the ring-A

(1) Part 1 of this series: Landucci, L. L.; Ralph, J. J. *J. Org. Chem.* 1982, 47, 3486.

(2) "Threo" and "erythro" are assigned in analogy with the parent models. See note 18 in Part 1 of this series (ref 1).

(3) Part 2 of this series: Ralph, J.; Landucci, L. L. *J. Org. Chem.* 1983, 48, 372.

(4) Fleming, I. *Chimia* 1980, 34(6), 265.

(5) Paterson, I. *Tetrahedron Lett.* 1979, 1519.

(6) Bromination of *erythro*-**3a** was stereospecific, producing *threo*-**5a** initially. This S_N2 behavior in S_N1 systems has been noted previously: Jung, M. E.; Hatfield, G. L. *Tetrahedron Lett.* 1978, 4483. Isomerization of *threo*-**5a** to an equilibrium mixture of 53:47 threo/erythro was presumably caused by HBr liberated during the reaction and was complete within 20 min.

(7) Adduct stereochemistry is independent of stereochemical purity of starting materials (**2**, **3**, or **5**) because of quinone methide or benzylic carbonium ion intermediates.

(8) *erythro*- and *threo*-**1a** and byproducts bromotrimethylsilane, hexamethyldisiloxane, and anthrone were the only compounds detected by 270-MHz ¹H NMR spectroscopy.

[†]This research was done while J.R. was a Ph.D. candidate in the Department of Forestry, University of Wisconsin, Madison, WI.

[‡]The laboratory is maintained at Madison, WI, in cooperation with the University of Wisconsin.

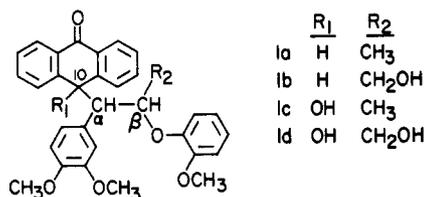


Figure 1. Structure of adducts.

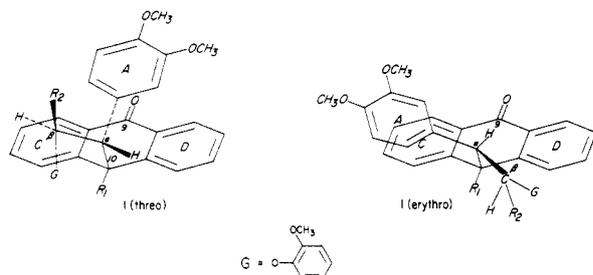


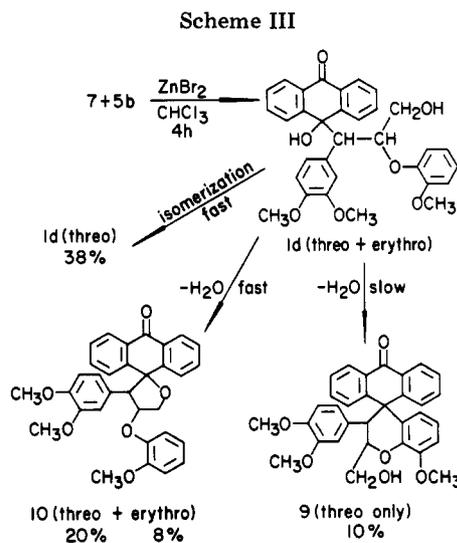
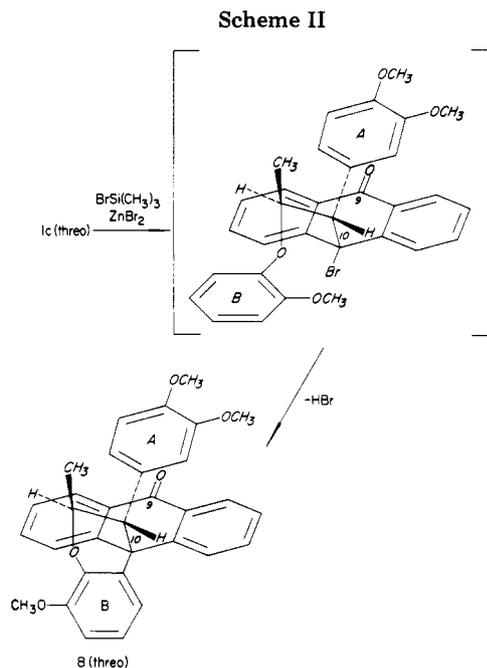
Figure 2. Conformation of threo and erythro isomers.

methoxys and ring protons by rings C and D and the dihedral angles indicated by the coupling constants $J_{10,\alpha}$ and $J_{\alpha,\beta}$ (Table I).

In contrast, the less intense shielding effects along with markedly different $J_{10,\alpha}$ values (Table I) for the erythro isomers are consistent with rotation about the C₁₀-C_α axis such that ring A is no longer situated over the plane of the anthracenyl moiety. Proposal of a specific conformation of the relatively unstable erythro isomers is difficult because of a high degree of bond rotation. This rotation is indicated by the significant changes in chemical shifts and coupling constants (particularly $J_{10,\alpha}$ and $J_{\alpha,\beta}$) that occur upon R₂ substitution (Figure 1) or solvent change (chloroform vs. acetone, Table I) and is in marked contrast to the rigid nature of the threo isomers.

Anthrahydroquinone Adducts. Alkylation of Me₃Si-AHQ (7) with 5a gave both isomers of 1c. Unfortunately, the threo/erythro ratio could not be conveniently monitored by ¹H NMR spectroscopy, as with the corresponding anthranol adducts 1a, because of severe line broadening caused by hindered rotation phenomena⁹ in the erythro adduct. However, an alkylation quenched after 2 min gave a combined yield of 85% 1c in a threo/erythro ratio of about 2:1 following thick-layer chromatography on silica gel. A minor component (5%) identified as the 10-trimethylsiloxy derivative of 1c was also isolated from the reaction mixture. This is presumably the first product formed from the reaction of 5a with 7. It was not determined whether the product was the threo or erythro isomer.

When the alkylation reaction was quenched after 5 min, only *threo*-1c was obtained. Therefore, complete isomerization of *erythro*-1c to *threo*-1c occurred within 5 min as compared to the 4-h isomerization noted for the corresponding anthranol adduct *erythro*-1a. The increased isomerization rate for *erythro*-1c can be explained by decreased stability caused by replacement of the C-10 proton of 1a (Figure 1) by the bulkier hydroxyl group. When the above alkylation was continued beyond the point of complete isomerization of *erythro*-1c to *threo*-1c (>5 min), the dehydration product *threo*-8 became prominent with concomitant disappearance of *threo*-1c (Scheme II). Dehydration of *threo*-1c was presumably initiated by bromination at the 10-position by bromotrimethylsilane regenerated from the silanated AHQ (7) (as seen by ¹H and



²⁹Si NMR) and catalyzed by the presence of the Lewis acid zinc bromide. The dehydration product is identical with one previously characterized,³ which was obtained by treatment of *threo*-1c with boron trifluoride etherate.

The last adduct (1d) of 7 was prepared by alkylation of 7 with 5b (2-min quench). A combined yield of about 70% *threo*-1d/*erythro*-1d was isolated in a ratio of 2:3 following thick-layer chromatography. The predominance of the erythro isomer in this case was unexpected and has not been explained. As with the corresponding anthranol adducts (1c), the mass and infrared spectra of both isomers are very similar. Only the ¹H NMR spectra reflect the markedly different conformations. Of particular interest is the extreme effect the solvent has on the ¹H NMR spectra of *erythro*-1d. In fact, its spectrum in CDCl₃ does not even resemble that in acetone-*d*₆ (Table I).

As expected from the preparations of anthranol adducts, longer alkylations (>5 min) resulted in reaction mixtures devoid of the erythro isomer. This can be explained not only by its isomerization to the more stable threo isomer but also by its facile conversion to a new dehydration product 10 (Scheme III).

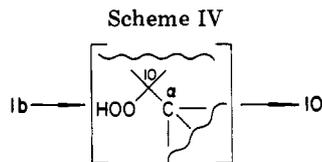
The threo isomer also generated this new product (10) in addition to the expected dehydration product 9 (anal-

(9) Kessler, H. *Angew. Chem., Int. Ed. Engl.* 1970, 9(3), 219.

Table I. ¹H NMR Data for Adducts^a

compound	solvent ^b	MHz	methoxyyls				ring A				rings C and D			
			A3	A4	B2	2	5	6	J ₅₆	J ₆₂	ring B	2-7	1,8	
			10H or 10-OH	γOH	γ1	β	γ2	J _{αβ}	J _{βγ2}	J _{γ1γ2}	J _{10α}			
<i>threo</i> -1a	C	270	3.33	3.72	4.01	5.30 (d)	6.34 (d)	5.44 (d)	8.5	1.8	7.01-7.12 (m)	7.32-7.79 (m)	7.90-8.05 (dd, dd)	
<i>erythro</i> -1a	C	270	3.84 ^c	3.84 ^c	3.87 ^c	7.05 ^d (h)	6.56 (d)	6.32 ^d (h)	8.1	?	6.62	7.45 (m)	8.08-8.17 (d, d)	
	A	270	3.67 ^c	3.82 ^c	3.71 ^c	^e	6.56 (d)	6.20 (bd)	8.1	?	6.74		8.05 (m)	
<i>threo</i> -1b	C	270	3.34	3.72	4.01	5.36 (bs)	6.34 (d)	5.47 (bd)	8.5	?	7.05-7.17 (m)	7.33-7.79 (m)	7.90-8.08 (d, d)	
<i>erythro</i> -1b	C	270	3.50 ^c	3.81 ^c	3.76 ^c	6.13 (bs)	6.44 (d)	5.91 (bd)	8.1	1.8	6.72	7.55 (m)	8.02-8.08 (m)	
	A	270	3.56 ^c	3.69 ^c	3.79 ^c	6.59 (bs)	6.51 (d)	6.09 (bd)	8.1	?	6.82	7.47 (m)	7.95-8.02 (m)	
<i>threo</i> -1c	A	270	3.36	3.64	4.02	5.60 (bs)	6.39 (d)	5.57 ^e	8.1	?	6.98-7.22 (m)	7.34-7.78 (m)	8.01-8.28 (dd, dd)	
<i>erythro</i> -1c	A	60	3.58 ^c (bs)	3.70 ^c	3.73 ^c	5.50 (bs)	6.53 (bd)	6.10 (bh)	8.5	?	6.8		8.4 (m)	
<i>threo</i> -1d	C	270	3.41 (bs)	3.73	4.01	5.5 (bh)	6.35 (d)	5.5 (bh)	8.1	?	6.87	7.90 (m)	8.10-8.28 (d, d)	
	A	270	3.35	3.64	4.01	5.63	6.38 (d)	5.61 (bd)	8.5	?	6.92	7.78 (m)	8.00-8.27 (d, d)	
<i>erythro</i> -1d	C	60	3.67 (bs)	3.80	3.90	5.2 (bh)	6.55 (bh)	5.2 (bh)	?	?	6.80	7.60 (m)	7.90-8.10 (m)	
	A	60	3.53 (bs)	3.67	3.67	5.47 ^d (bs)	6.45 (bd)	5.2 ^d (bh)	8.0	?	6.85		8.10 (m)	
<i>threo</i> -9	C	270	3.28 (bs)	3.72	4.01	5.41 ^d (bh)	6.29 ^e	5.04 ^d (bh)	?	?	6.29-6.84 (d, dd, d)	7.26-7.57 (m)	8.01-8.07 (m)	
	A + D	270	3.25 (bs)	3.66	3.99	5.47 ^d (h)	6.38 (d)	5.18 ^d (h)	7.7	?	6.18-7.06 (d, dd, d)	7.26-7.68 (m)	7.97-8.00 (m)	
<i>threo</i> -10	C	270	3.32	3.76	3.82	6.32 (d)	6.43 (d)	5.95 (dd)	8.1	2.2	6.67		8.23 (m)	
	A	270	3.25	3.64	3.87	6.30 (d)	6.44 (d)	5.94 (dd)	8.1	2.2	6.83		8.26 (m)	
<i>erythro</i> -10	C	270	3.33	3.68	3.72	5.54 (d)	6.39 (d)	5.80 (dd)	8.1	1.8	6.75-6.94 (m)	7.29-7.82 (m)	8.04-8.08 (d, d)	
	A	270	3.30	3.64	3.70	5.68 (d)	6.44 (d)	5.82 (dd)	8.1	2.2	6.73-6.96 (m)	7.39-8.18 (m)	8.28-8.32 (d, d)	
compound	solvent ^b	MHz	10H or 10-OH	γOH	γ1	β	α	γ2	J _{αβ}	J _{βγ2}	J _{γ1γ2}	J _{10α}		
<i>threo</i> -1a	C	270	5.37 (d)	2.49 (dd)	3.42 (dd)	4.77 (dq)	3.42 (dd)	1.07 (d)	10.7	5.9		3.3		
<i>erythro</i> -1a	C	270	4.67 (d)	2.77 (dd)	2.49 (dd)	4.36 (dq)	2.49 (dd)	0.98 (d)	4.0	6.3		9.2		
	A	270	4.78 (d)	2.77 (dd)	2.77 (dd)	4.60 (dq)	2.77 (dd)	1.12 (d)	4.8	6.3		7.7		
<i>threo</i> -1b	C	270	5.28 (d)	2.49 (h)	3.81 (dd)	4.57 (bd)	3.81 (dd)	3.10 (bd)	11.0	?	2.6	2.9		
<i>erythro</i> -1b	C	270	4.75 (d)	2.52 (h)	3.42 (dd)	4.45 (m)	3.42 (dd)	3.9 (m)	8.1	?	?	5.5		
	A	270	4.85 (d)	?	3.31 (dd)	4.58 (ddd)	3.31 (dd)	3.54 (dd)	5.9	6.8	4.0	6.4		
<i>threo</i> -1c	A	270	?	?	3.51 (d)	4.83 (dq)	3.51 (d)	1.03 (d)	10.3	5.9				
<i>erythro</i> -1c	A	60	2.78	?	3.05 (d)	?	3.05 (d)	1.00 (d)	2.2	6.0				
<i>threo</i> -1d	C	270	6.71	2.28 (h)	3.88 (d)	4.54 (bd)	3.88 (d)	3.02 (h)	11.0	?	?	12.5		
	A	270	6.98	2.88 (bs)	3.92 (d)	4.74 (bd)	3.92 (d)	3.11 (dd)	10.7	2.2	2.2	12.5		
<i>erythro</i> -1d	C	60	?	?	3.02 (d)	4.50 (m)	3.02 (d)	?	3.2	?	?	?		
	A	60	2.80 (bs)	?	?	?	?	?	?	?	?	?		
<i>threo</i> -9	C	270	2.37 (bh)	2.80 (bs)	?	4.74 (m)	3.43 (d)	3.46 ^e	11.4	?	?	?		
	A + D	270		2.37 (bh)	?	4.80 (m)	3.51 (d)	3.43 (dd)	11.4	5.5	?	?		
<i>threo</i> -10	C	270		2.37 (bh)	?	5.17 (dd)	3.54 (d)	4.84 (dd)	4.4	3.3	<1	12.5		
	A	270		2.37 (bh)	?	5.31 (dd)	3.66 (d)	4.90 (dd)	4.4	<1	2.9	10.3		
<i>erythro</i> -10	C	270		2.37 (bh)	?	5.25 (m)	3.77 (d)	4.66 (dd)	10.3	8.1	7.0	8.4		
	A	270		2.37 (bh)	?	5.54 (m)	3.73 (d)	4.58 (dd)	10.3	8.1	7.0	8.4		

^a Chemical shifts in ppm relative to Me₄Si, *J* values in Hz, peaks are sharp singlets unless otherwise designated. Abbreviations: bs = broad singlet, bd = broad doublet, bh = broad hump, d = doublet, dd = double doublet, ddd = doublet of doublets, dq = doublet of quartets, h = hump, m = multiplet. ^b C = CDCl₃, A = acetone-*d*₆, D = D₂O. ^c Methoxyyl assignments may be interchangeable. ^d Interchangeable because of hindered rotation of ring A. ^e Partially hidden.



ogous to 8, Scheme II). The fact that no *erythro*-9 (or *erythro*-8) was ever detected in alkylation mixtures is not surprising considering that this dehydration pathway is relatively slow compared to the rate of isomerization of *erythro*-AHQ adducts to *threo*-AHQ adducts.

The proposed structures of 9 and both isomers of 10 are consistent with NMR and mass spectroscopy data. It was found that 10 could also be prepared from the anthrone adduct 1b. Treatment of 1b with alkali followed by extraction into chloroform in the presence of air gave a quantitative yield of 10. Furthermore, *erythro*-1b gave *erythro*-10 and *threo*-1b gave *threo*-10. Although the mechanism has not been investigated, it may involve a transient hydroperoxy species because workup in the absence of air gave only starting material (Scheme IV).

In summary, the successful synthesis of erythro adducts between AHQ or anthranol and lignin models enabled comparisons with corresponding threo adducts, which are representative of intermediates responsible for catalytic delignification of wood in the presence of AHQ. Remarkable differences in the conformation and stability of the threo and erythro adducts were found. The fact that erythro adducts were not detected under alkaline conditions^{1,3,10} and are much less stable than threo adducts suggests that they have no role in alkaline delignification. However, the existence of another isomeric form with very different properties illustrates the need to exercise caution when describing lignin reactions on the basis of model studies in which stereochemistry is ignored.

Experimental Section

¹H NMR spectra were determined in CDCl₃ or acetone-*d*₆ on a Varian T-60 or a Bruker WH270 spectrometer with Me₄Si as internal reference (the 270-MHz spectra were run with 16K data points resulting in *J* values accurate to ±0.4 Hz). ¹³C NMR spectra were determined in CDCl₃ or acetone-*d*₆ on a JEOL FX60 (15 MHz) or JEOL FX200 (50.1 MHz) spectrometer. Assignment ambiguities were resolved either by single-frequency off-resonance decoupling (SFORD) techniques or by broad-band proton-decoupled ¹³C INEPT pulse sequencing using $\tau = 1/4 J$ and a delay, $\Delta = 3/4 J$ (inversion of CH₂ resonances).^{11,12} ²⁹Si NMR spectra were recorded with a JEOL FX 200 (39.6 MHz) spectrometer using a broad-band proton-decoupled ²⁹Si INEPT pulse sequence¹³ with $\tau = \Delta = 1/4 J$. ²⁹Si-¹H coupling constants were determined from coupled INEPT spectra. Infrared spectra of samples in KBr disks or films were determined on a Beckman IR-12 spectrometer. Mass spectra were determined with a solid probe on a Varian MAT 112 spectrometer (Raltech Scientific Services, Inc.) or a Finnigan 4510 GC/MS. All methane and isobutane CI spectra were run at 0.5 torr. Melting points were determined on a calibrated Thomas-Hoover capillary melting point apparatus. Compounds were purified by thick-layer chromatography on silica gel using 5–50% ethyl acetate/hexane or chloroform as developer. Methylations were accomplished with diazomethane in methanol/diethyl ether. Acetylations were performed with 1:1 acetic anhydride/pyridine (often containing a trace of (dimethylamino)pyridine as catalyst).

Preparation of Starting Materials. Lignin Models. 1-(3,4-Dimethoxyphenyl)-2-(2-methoxyphenoxy)propan-1-ol (3a). Prepared according to a literature procedure.¹⁴

1-(3,4-Dimethoxyphenyl)-2-(2-methoxyphenoxy)propane-1,3-diol (3b). Prepared according to a literature procedure.¹⁵

Trimethylsilyl Enol Ethers. Prepared by methods similar to literature procedures.^{16,17}

(Trimethylsilyl)anthranol [9-(Trimethylsilyloxy)anthracene] (6). Anthrone (2.0 g, 10 mmol) was added to a solution of chlorotrimethylsilane (1.4 g, 13 mmol) and triethylamine (2.6 g, 26 mmol) in dimethylformamide (10 mL). The mixture was refluxed with stirring for 48 h, cooled, and poured into hexane. The hexane layer was washed three times with cold aqueous NaHCO₃, twice with cold 5% HCl, and three times with NaHCO₃ again, then dried over MgSO₄, and filtered. Evaporation of the solvent left a crystalline product: 2.5 g, 9.5 mmol, 95%; mp 103.5–105 °C (lit.¹⁸ mp 105–106 °C); ¹H NMR (60 MHz, CDCl₃) δ 0.33 (s, Me₃Si methyls), 7.15–7.55 (m, H 2, 3, 6, 7 aromatics), 7.7–8.3 (m, H 1, 4, 5, 8, 9 aromatics); ²⁹Si NMR (39.6 MHz, CDCl₃) δ 23.2 (²*J*_{Si,H} = 6.7 ± 1).

(Trimethylsilyl)anthrahydroquinone [9,10-Bis(trimethylsilyloxy)anthracene] (7). AHQ, prepared from anthraquinone (1.3 g, 6.3 mmol), as described previously,¹ was suspended in triethylamine (30 mL) and dimethylformamide (10 mL). Chlorotrimethylsilane (16 g) was added and the solution refluxed for 12 h. Workup as in the previous preparation gave a crude solid: 1.1 g, 3.1 mmol, 49%. Sublimation under vacuum gave pale yellow crystals: mp 123–125 °C (lit.¹⁹ mp 124–125 °C); ¹H NMR (60 MHz, CDCl₃) δ 0.32 (s, methyls), 7.2–7.5 (m, H 2, 3, 6, 7 aromatics), 8.0–8.3 (m, H 1, 4, 5, 8 aromatics); ²⁹Si NMR (39.6 MHz, CDCl₃) δ 23.0; MS (EI, 50 eV), *m/e* (relative intensity) 354 (M⁺, 100), 339 (8), 265 (9), 235 (6), 207 (7).

Bromotrimethylsilane. Obtained from Aldrich Chemical Co.: ¹H NMR (270 MHz, CDCl₃) δ 0.58 (s); ²⁹Si NMR (39.6 MHz, CDCl₃) δ 26.4.

Hexamethyldisiloxane. Prepared by adding excess benzyl alcohol or water to bromotrimethylsilane: ¹H NMR (270 MHz, CDCl₃) δ 0.07 (s); ²⁹Si NMR (39.6 MHz, CDCl₃) δ 7.1 (s).

Bromination of Lignin Models. General Procedure Illustrated for 3a. The lignin model 3a (20–100 mg) was dissolved in CHCl₃ (5–20 mL), and trimethylsilyl bromide (2 equiv) was added under N₂. After approximately 1 min, the solution was poured into saturated NaHCO₃ and extracted with CHCl₃. The organic layer was dried over MgSO₄ and filtered, and the solvent was removed, leaving the bromide 5a as a pale yellow oil in quantitative yield.

1-Bromo-1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)propane (5a): ¹H NMR (270 MHz, CDCl₃) threo isomer, δ 1.50 (d, *J* _{$\gamma\beta$} = 6.3, γ CH₃), 3.75, 3.83, 3.85 (3 s, methoxyls), 4.74 (dq, *J* _{$\beta\gamma$} = 6.3, *J* _{$\beta\alpha$} = 5.9, H β), 5.10 (d, *J* _{$\alpha\beta$} = 5.9, H α), 6.74–7.01 (m, aromatics); erythro isomer, δ 1.24 (d, *J* _{$\beta\gamma$} = 6.3, γ -CH₃), 3.86, 3.87, 3.88 (3 s, methoxyls), 4.74 (dq, *J* _{$\beta\gamma$} = 6.3, *J* _{$\beta\alpha$} = 6.6, H β), 5.13 (d, *J* _{$\alpha\beta$} = 6.6 H α), 6.74–7.01 (m, aromatics).

1-Bromo-1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)propan-3-ol (5b): ¹H NMR (60 MHz, CDCl₃) 1:1 threo/erythro mixture, δ 3.4–4.2 (m, methoxyls, H γ s, OHs), 4.3–4.8 (m, H β s), 5.27 (d, *J* _{$\alpha\beta$} \approx 8.5, threo H α), 5.35 (d, *J* _{$\alpha\beta$} \approx 9, erythro H α) 6.8–7.4 (m, aromatics).

Alkylations: General Procedure. Bromide 5a or 5b (20–80 mg) was dissolved in CDCl₃ (0.5 mL) in a 5-mm NMR tube. 6 or 7 (2 equiv) was added, and a ¹H NMR spectrum was run to check the starting materials. Then 10–20 mg of anhydrous ZnBr₂ was added, the tube vigorously shaken, and another spectrum taken. Adduct formation was generally complete within the time required to obtain a spectrum (<2 min). The silicon species were also followed in selected runs by ²⁹Si NMR spectroscopy. Reactions were worked up by pouring the reaction mixture into saturated NaHCO₃ solution, followed by extraction with diethyl ether. The ether layer was dried over MgSO₄ and filtered, and

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the solvent was removed, leaving an oil, the components of which were separated by thick-layer chromatography on silica gel.

1-(3,4-Dimethoxyphenyl)-1-(9,10-dihydro-9-oxoanthracen-10-yl)-2-(2-methoxyphenoxy)propane (1a). Reaction of **5a** with Me_3Si **6** by the general procedure gave **1a** (initial *threo*/*erythro* ratio of 3:2 determined by ^1H NMR) along with byproducts anthrone, bromotrimethylsilane, and hexamethyldisiloxane. Chromatography of the crude reaction mixture on silica gel gave *threo*-**1a** as a pale yellow oil [^1H NMR (Table I); ^{13}C NMR (50.1 MHz, CDCl_3) δ 18.6 ($\gamma\text{-CH}_3$), 44.0 (C10), 55.7, 55.7, 56.1 (methoxyls), 63.4 ($C\alpha$), 74.0 ($C\beta$), 110.6–115.7 (C2, 5, ring A; C3, 6, ring B), 121.2–122.1 (C6, ring A; C4, 5, ring B), 126.3–135.0 (C1-8, 8a, 9a, anthracenyl; C1, ring A), 141.1–148.5 (C3, 4, ring A; C2, ring B; C4a, 10a, anthracenyl), 150.8 (C1, ring B), 183.3 (C9)]; MS (EI, 80 eV), *m/e* (relative intensity) 494 (M^+ , 0.2), 370 (1.0), 301 (45), 193 (17), 178 (100), 163 (50), 123 (9); IR (film) 1672 vs cm^{-1} (C=O)] and *erythro*-**1a** as pale yellow platelets [mp 112–113.5 °C; ^1H NMR (Table I); ^{13}C NMR (50.1 MHz, CDCl_3) δ 17.8 ($\gamma\text{-CH}_3$), 48.2 (C10), 55.8 (methoxyls), 64.9 ($C\alpha$), 73.3 ($C\beta$), 120.8–123.3 (C6, ring A; C4, 5, ring B), 126.7–133.2 (C1-8, 8a, 9a, anthracenyl; C1, ring A), 144.1–148.7 (C3, 4, ring A; C2, ring B; C4a, 10a, anthracenyl), 150.4 (C1, ring B), 185.8 (C9)]; MS (EI, 80 eV), *m/e* (relative intensity) 494 (M^+ , 0.2), 370 (0.1), 301 (33), 194 (26), 193 (19), 178 (100), 163 (64), 123 (10); IR (film) 1671 vs cm^{-1} (C=O)].

1-(3,4-Dimethoxyphenyl)-1-(9,10-dihydro-9-oxoanthracen-10-yl)-2-(2-methoxyphenoxy)propan-3-ol (1b). Reaction of **5b** with **6** according to the general procedure (20-min reaction) gave **1b** in quantitative yield with a *threo*/*erythro* ratio of 2:1. Separation of the isomers on silica gel (multiple elution with 10–20% ethyl acetate/hexane) gave *threo*-**1b** as white crystals [mp 135–137 °C; ^1H NMR (Table I); ^{13}C NMR (50.1 MHz, CDCl_3) δ 43.7 (C10), 55.8, 56.1, 56.7 (methoxyls), 57.0 ($C\alpha$), 60.9 ($C\gamma$), 80.1 ($C\beta$), 110.8–113.6 (C2, 5, ring A; C3, ring B), 118.3 (C6, ring B), 121.7–123.4 (C6, ring A; C4, 5, ring B), 126.3–135.2 (C1-8, 8a, 9a, anthracenyl; C1, ring A), 141.2–148.7 (C3, 4, ring A; C2, ring B; C4a, 10a, anthracenyl), 151.3 (C1, ring B), 183.2 (C9)]; MS (EI, 70 eV), *m/e* (relative intensity) 510 (M^+ , 0.01), 368 (0.1), 317 (15), 287 (11), 194 (55), 193 (71), 179 (12), 176 (38), 165 (37), 164 (31), 151 (100), 149 (41), 138 (23), 123 (24); IR (film) 3530 m (sharp, OH), 1670 s (C=O) cm^{-1}] and *erythro*-**1b** as white crystals [mp 188–188.5 °C; ^1H NMR (Table I); ^{13}C NMR (50.1 MHz, CDCl_3) δ 46.3 (C10), 55.5, 55.9, 55.9 (methoxyls), 58.4 ($C\alpha$), 61.7 ($C\gamma$), 81.5 ($C\beta$), 110.5–113.7 (C2, 5, ring A; C3, ring B), 117.9 (C6, ring B), 121.2–122.8 (C6, ring A; C4, 5, ring B), 126.9–134.1 (C1-8, 8a, 9a, anthracenyl; C1, ring A), 142.6–148.2 (C3, 4, ring A; C2, ring B; C4a, 10a, anthracenyl), 151.1 (C1, ring B), 184.1 (C9)]; MS (EI, 70 eV), *m/e* (relative intensity) 510 (M^+ , 0.01), 318 (20), 317 (17), 299 (19), 287 (14), 195 (42), 194 (61), 193 (81), 176 (60), 165 (56), 164 (29), 152 (41), 151 (100), 150 (25), 149 (39), 138 (25), 123 (34); IR (film) 3520 m (br, OH), 1670 s (C=O) cm^{-1}].

1-(3,4-Dimethoxyphenyl)-1-(9,10-dihydro-9-oxo-10-hydroxyanthracen-10-yl)-2-(2-methoxyphenoxy)propane (1c). Reaction of **5a** with **7** according to the general procedure (2-min reaction) gave *threo*/*erythro*-**1c** (2:1 ratio) in a combined yield of 85% following purification on silica gel. *threo*-**1c**: colorless oil; ^1H NMR (Table I); ^{13}C NMR, reported previously;¹ MS (EI, 50 eV), *m/e* (relative intensity) 301 (5), 209 (8), 178 (100), 163 (19); MS (CI, CH_4 , 25 eV), *m/e* (relative intensity) 539 ($\text{M} + 29$, 0.1), 511 ($\text{M} + 1$, 0.1), 493 ($\text{M} + 1 - \text{H}_2\text{O}$, 0.7), 343 (10), 301 (81), 237 (10), 209 (83), 179 (100), 178 (19), 165 (14), 125 (76); MS (CI, $i\text{-C}_4\text{H}_{10}$, 40 eV), *m/e* (relative intensity) 511 ($\text{M} + 1$, 0.1), 494 (0.3), 493 ($\text{M} + 1 - \text{H}_2\text{O}$, 1.1), 343 (7), 301 (63), 209 (68), 179 (100), 178 (13), 125 (16). *erythro*-**1c**: colorless oil; ^1H NMR (Table I); ^{13}C NMR, very obscure due to hindered rotation phenomenon;⁹ MS (EI, 50 eV), *m/e* (relative intensity) 301 (9), 209 (9), 178 (100), 163 (23); MS (CI, CH_4 , 25 eV), *m/e* (relative intensity) 539 ($\text{M} + 29$, 0.2), 511 ($\text{M} + 1$, 0.1), 387 (0.6), 343 (8), 301 (81), 237 (9), 209 (76), 179 (100), 178 (20), 165 (12), 125 (70); MS (CI, $i\text{-C}_4\text{H}_{10}$, 40 eV), *m/e* (relative intensity) 511 ($\text{M} + 1$, 0.1), 493 ($\text{M} + 1 - \text{H}_2\text{O}$, 0.1), 387 (0.2), 343 (3), 301 (34), 209 (58), 179 (100), 178 (11), 125 (18). A minor component (5%) in the reaction mixture was identified as the 10-trimethylsilyloxy derivative of **1c**: MS (EI, 50 eV), *m/e* (relative intensity) 582 (M^+ , 0.02), 443 (0.03), 355 (1), 202 (11), 301 (54), 282 (33), 281 (20), 178 (100), 177 (5), 163 (34), 123 (6), 107 (5), 73 (40).

1-(3,4-Dimethoxyphenyl)-1-(9,10-dihydro-9-oxo-10-hydroxyanthracen-10-yl)-2-(2-methoxyphenoxy)propan-3-ol (1d). Reaction of **5b** with **7** according to the general procedure (2-min reaction) gave *threo*/*erythro*-**1d** (2:3 ratio) in a combined yield of 70% following CHCl_3 elution on silica gel. *threo*-**1d**: pale yellow oil; ^1H NMR (Table I); ^{13}C NMR (50.1 MHz, acetone- d_6) δ 55.7, 56.2, 56.5 (methoxyls), 61.2 ($C\alpha$), 61.4 ($C\gamma$), 77.6 (C10), 82.5 ($C\beta$), 112.3–116.0 (C2, 5, ring A; C3, 6, ring B), 121.9–133.9 (C1, 6, ring A; C4, 5, ring B; C1-4, ring C; C8a, 9a; C5-8, ring D), 145.3–149.7 (C3, 4, ring A; C2, ring B; C4a, 10a), 151.0 (C1, ring B), 182.6 (C9); IR (film) 3480 s (br, OH), 1670 s (C=O) cm^{-1} ; MS (EI, 50 eV), *m/e* (relative intensity) 318 (2), 317 (1), 299 (3), 287 (3), 210 (11), 209 (21), 208 (17), 194 (82), 180 (18), 176 (14), 165 (12), 164 (13), 152 (36), 151 (100), 150 (10), 149 (17), 138 (23), 124 (16), 123 (12), 109 (14); MS (CI, $i\text{-C}_4\text{H}_{10}$, 40 eV), *m/e* (relative intensity) 527 ($\text{M} + 1$, 0.02), 512 (0.03), 511 (0.1), 509 ($\text{M} + 1 - \text{H}_2\text{O}$, 0.8), 317 (9), 209 (97), 195 (92), 177 (100), 125 (29). *erythro*-**1d**: colorless oil; ^1H NMR (Table I); ^{13}C NMR very obscure due to hindered rotation phenomenon;⁹ MS (EI, 70 eV), *m/e* (relative intensity) 318 (2), 317 (2), 299 (4), 287 (6), 210 (11), 209 (15), 208 (29), 194 (76), 193 (11), 180 (27), 176 (17), 165 (11), 164 (14), 152 (33), 151 (100), 150 (10), 149 (19), 138 (16), 124 (19), 123 (13), 109 (19); MS (CI, $i\text{-C}_4\text{H}_{10}$, 40 eV), *m/e* (relative intensity) 509 ($\text{M} + 1 - \text{H}_2\text{O}$, 0.01), 317 (1), 209 (93), 195 (57), 177 (100), 125 (28).

When the previous alkylation was carried out for 4 h rather than 2 min, no *erythro*-**1d** was found in the reaction mixture. The major components were *threo*-**1d** (38%), *threo*-**9** (10%), *threo*-**10** (20%), and *erythro*-**10** (8%).

***threo*-3'-(3,4-Dimethoxyphenyl)-2',3'-dihydro-8'-methoxy-2'-hydroxymethylspiro[anthracen-9(10H),4'-(4H-1)benzopyran]-10-one (9):** white crystals; mp 229–229.5 °C; ^1H NMR (Table I); ^{13}C NMR (50.1 MHz, CDCl_3) δ 51.1 (C10), 55.6, 55.8, 56.0, 56.4 ($C\alpha$, methoxyls), 63.9 ($C\gamma$), 75.5 ($C\beta$), 110.3–133.7 (C1, 2, 5, 6, ring A; C2-6, ring B; C1-4, ring C; C5-8, ring D; C8a, 9a), 145.2–148.9 (C3, 4, ring A; C1, 2, ring B; C4a, 10a), 181.8 (C9); MS (EI, 50 eV), *m/e* (relative intensity) 508 (M^+ , 2), 327 (14), 314 (34), 299 (12), 285 (12), 271 (22), 255 (22), 215 (11), 194 (19), 165 (16), 164 (12), 151 (100), 138 (32), 107 (10); IR (film) 3500 w (br, OH), 1670 s (C=O) cm^{-1} .

4',5'-Dihydro-3'-(3,4-dimethoxyphenyl)-4'-(2-methoxyphenoxy)spiro[anthracen-9(10H),2'(3'H)-furan]-10-one (10). Three isomer: pale yellow crystals; mp 155–157 °C; ^1H NMR (Table I); ^{13}C NMR (15.1 MHz, acetone- d_6) δ 55.3, 56.7, (methoxyls), 66.9 ($C\alpha$), 76.6 ($C\gamma$, inverted by $\tau = ^3J_{\text{H-C}}$ INEPT), 81.5 ($C\beta$), 87.8 (C10, not observed by INEPT), 111.0–116.2 (C2, 5, ring A; C3, 6, ring B), 121.3–134.0 (C1, 6, ring A; C4, 5, ring B; C5, ring D; C8a, 9a), 145.2–150.3 (C3, 4, ring A; C2, ring B; C4a, 10a), 150.9 (C1, ring B), 182.7 (C9); MS (EI, 50 eV), *m/e* (relative intensity) 508 (M^+ , 0.3), 177 (100), 176 (55), 146 (13), 123 (3); IR (film) 1680 s cm^{-1} (C=O). *erythro* isomer as white crystals: mp 196.5–197.0 °C; ^1H NMR (Table I); ^{13}C NMR (50.1 MHz, acetone- d_6) δ 55.6, 55.9, 55.9 (methoxyls), 66.6 ($C\alpha$), 73.6 ($C\gamma$), 82.0 ($C\beta$), 86.1 (C10), 111.0–112.9 (C2, 5, ring A; C3, ring B), 119.9 (C6, ring B), 121.1–134.1 (C1, 6, ring A; C4, 5, ring B; C1-4, ring C; C5, ring D; C8a, 9a), 144.7–149.2 (C3, 4, ring A; C2, ring B; C4a, 10a), 151.4 (C1, ring B), 182.3 (C9); MS (EI, 50 eV), *m/e* (relative intensity) 508 (M^+ , 0.3), 208 (2), 180 (3), 177 (100), 176 (52), 146 (28), 123 (2); IR (film) 1674 s cm^{-1} (C=O).

Independent Syntheses of Both Isomers of 10. Each isomer of compound **1b** reacted stereospecifically to give the corresponding isomer of **10** according to the following procedure illustrated for the *threo* isomer. A 5% solution of sodium hydroxide (6 mL) was added to a solution of *threo*-**1b** (77 mg) in dioxane (4 mL). The resulting solution was heated at 80 °C in an open flask for 2 h, after which the reaction mixture was cooled, transferred to a separatory funnel with CHCl_3 (20 mL), and vigorously shaken with air for several minutes. The chloroform solution was separated and dried over MgSO_4 , and the solvent was removed, leaving a quantitative yield of product that was found to be identical with *threo*-**10** isolated from the previous alkylation reaction.

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Registry No. (*R*,R**)-1a, 82247-15-2; (*R*,S**)-1a, 86956-00-5; (*R*,R**)-1b, 86956-01-6; (*R*,S**)-1b, 86956-02-7; (*R*,R**)-1c,

82247-06-1; (*R*,S**)-1c, 86956-03-8; 1c 10-trimethylsilyloxy derivative, 86956-04-9; (*R*,S**)-1d, 86968-53-8; (*R*,R**)-1d, 86968-54-9; (*R*,R**)-3a, 36483-10-0; (*R*,S**)-3a, 7107-92-8; (*R*,R**)-3b, 7595-29-1; (*R*,S**)-3b, 7572-98-7; (*R*,R**)-5a, 86956-05-0; (*R*,S**)-5a, 86956-06-1; (*R*,R**)-5b, 86956-07-2; (*R*,S**)-5b, 86956-08-3; 6, 28871-54-7; 7, 28871-52-5; *trans*-9, 86956-09-4; *trans*-10, 86956-10-7; *cis*-10, 86956-11-8; lignin, 9005-53-2.

Reactions of Azines. 6. Thermal Rearrangements of 1,1-Disubstituted-2,3-diaza-4-methyl-1,3,5,6-heptatetraene to 4,9-Dihydropyrazolo[1,5-*b*]isoquinolines and Side Products

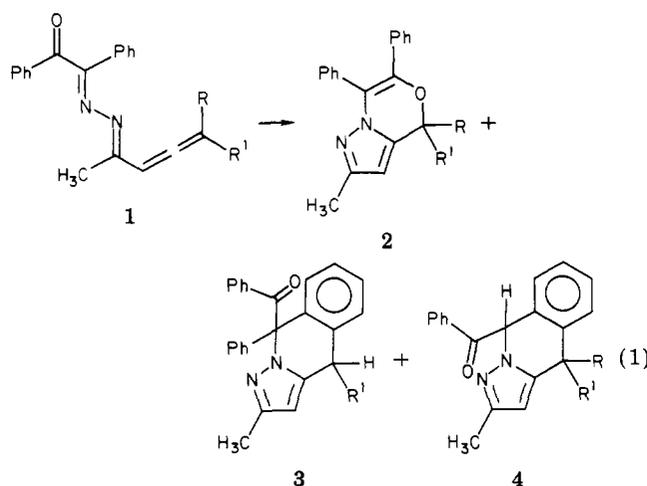
Edward E. Schweizer,* Weiling Hsueh, Arnold L. Rheingold,[†] and Rebecca L. Durney[†]

Department of Chemistry, University of Delaware, Newark, Delaware 19711

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The preparation of 4,9-dihydropyrazolo[1,5-*b*]isoquinolines (16 or/and 18) was accomplished by allowing the corresponding ketenes to react with 2-((diphenylmethylene)hydrazono)propylidene)triphenylphosphorane (10) and 2-((methylphenylmethylene)hydrazono)propylidene)triphenylphosphorane (11). It was determined that the predicted stability of the carbocation of the intermediate azomethine imine 15, or 17, on the 1- and 5-positions on the pyrazole backbone allowed one to predict the major product 16 or 18 of the reaction. An X-ray analysis of the thermodynamically more stable product of the reaction of phenylketene with ylide 10 showed it to be in the *trans* geometry, 18d-1, with the three central rings essentially planar (170.7° angle) about the C-4/C-9 axis.

The usefulness of di- α,β -unsaturated azines as synthons for a variety of N-substituted pyrazoles^{1a-e} as well as tetrahydroindazoles,^{1b} pyrazolopyrans,^{1b} and cyclopentapyrazoles^{1b} has been demonstrated. It has also been shown that keto allenyl azines, 1, when R = H (R¹ = H, vinyl, Ph), give exclusively pyrazolo[5,1-*c*]-1,4-oxazines, 2, whereas when the allenyl substituents are not hydrogen and one of the R's is phenyl, the major products are pyrazolo-oxazines, 2, and 4,9-dihydropyrazolo[1,5-*b*]isoquinolines, 3, and at times 4.²

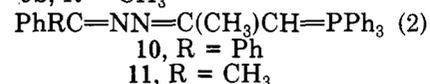
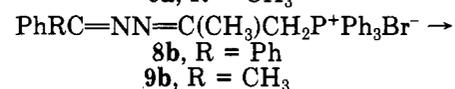
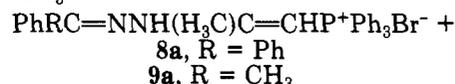
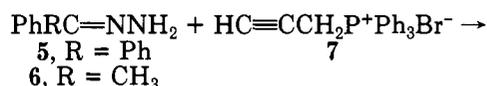


In an attempt to develop a method for the preparation of 4,9-dihydropyrazolo[1,5-*b*]isoquinolines without the inclusion of the pyrazolo[5,1-*c*]-1,4-oxazine side products, we examined the reactions of allenyl-substituted azines without a carbonyl or π system (other than the aromatic

moiety) at the other end of the azine from the allenyl group.

Results and Discussion

The hydrazones of benzophenone and acetophenone were allowed to react with propargyltriphenylphosphonium bromide (7) to give 2-((diphenylmethylene)hydrazono)propyltriphenylphosphonium bromide (8) and 2-((methylphenylmethylene)hydrazono)propyltriphenylphosphonium bromide (9). The ³¹P NMR spectrum



clearly showed that the predominant form of both 8 and 9 is the N-substituted vinylphosphonium species 8a and 9a. The ratios found were 8a/8b = 2/1 and 9a/9b = 3/1. The isomers of 8a showed ³¹P NMR in the 15.8–16.7 ppm range and 9a at 16.8–17.8 ppm, whereas the 8b (azine methylphosphonium) isomers showed ³¹P NMR at 22.1

[†] For X-ray structure.

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